REMARKS/ARGUMENTS

Upon entry of the present amendments, claims 32, 35-40, and 42-43 are pending. Claims 33-34, and 41 have been cancelled, without prejudice. Claim 43 is a new claim. The bases for the Office's rejection of claims 32, and 35-40, and 42 are addressed below. The foregoing amendments are made without any intention to abandon any subject matter of these claims, but with the intention that claims of the same, lesser, or greater scope may be pursued in a later application or in a continuation, continuation-in-part, or divisional application. The present amendment does not add new matter.

Amended claims 32, 35-40, and 42 are supported by at least the claims as originally filed and the specification, *e.g.*, page 1, line 11; page 3, line 13; page 4, line 9; page 5, line 7; and page 6, lines 15-28 through page 7, lines 1-23. New claim 43 is supported by at least the claims as originally filed and the specification, *e.g.*, page 5, lines 5-10.

35 U.S.C. § 112, First Paragraph Rejections

The Office has rejected claims 32-42 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification because claims 32-42 recited an element required for antibody secretion. The Office has also rejected claims 32-42 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification in such a way as to reasonably convey to the skilled artisan that the Applicants had possession of the claimed invention at the time of filing. Specifically, the recitation of 'coding for a native, unmodified antibody molecule' was alleged to be new matter (*see,* page 6, lines 10-17). Applicants note that, in the April 10, 2002 Office Action, the recitation objected to in the present rejection was recitation that was proposed by the Examiner as "a more literal and proper translation" of a passage in the Specification. See, page 4 of the April 10, 2002 Office Action.

The rejection of claims 33-34, and 41 are moot as these claims have been cancelled. Applicants respectfully traverse the rejection of claims 32, 35-40, and 42 for the reasons stated.

The Examiner has correctly concluded that "the specification generally supports the secretion of the translated antibody produced" (*see,* page 5, lines 16-18 of the instant Office Action). Claims 32, 35-40, and 42 have been amended to delete the recitation alleged to be new matter and to recite that the antibody is secreted into the blood circulation upon implantation or that the translation of the polynucleotide encoding the therapeutic antibody of the present invention results in the secretion of the antibody polypeptide from the mammalian nonplasmocyte cell into the blood circulation of a host mammal after the implantation of the cell.

The Examiner has also observed that, "the specification generally supports the expression of a therapeutic antibody" (*see,* page 7, line 5). Claims 32, 35-40, and 42 have been amended and are directed to expression of therapeutic antibodies wherein the polynucleotide sequences encoding the antibody have not been modified.

In view of the above described amendments, Applicants respectfully request withdrawal of the rejection of pending claims 32, and 35-40, and 42 under 35 U.S.C. § 112, first paragraph, and reconsideration of the claims in view of the same.

35 U.S.C. § 112, SECOND PARAGRAPH REJECTIONS

The Office has also rejected claims 32-42 under 35 U.S.C. § 112, second paragraph, alleging the claims are indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as their invention. The Office stated that the recitation of 'coding for a native, unmodified antibody molecule' was alleged to be new matter (*see,* page 6, lines 10-17). The Office stated that it was unclear whether the claims encompassed fragments of the complete antibody molecules because dependent claims 34 and 41 indicated that the contemplated sequences are fragments. The Office also stated that the recitation of 'is suitable' was unclear.

The rejection of claims 33-34, and 41 are moot as these claims have been cancelled. Applicants respectfully traverse the rejection of claims 32, 35-40, and 42 for the reasons stated.

Claim 32, 40, and 42 have been amended to delete the recitation 'is suitable.' Furthermore, dependent claims 34 and 41 have been deleted and the language of claims 32 and 40 have been amended to clarify that the claims only encompasses complete antibody molecules and not fragments thereof.

In view of the above described amendments, Applicants respectfully request withdrawal of the rejection of pending claims 32, 35-40, and 42 under 35 U.S.C. § 112, second paragraph, and reconsideration of the claims in view of the same.

35 U.S.C. § 102 REJECTION (WRIGHT *ET AL.*)

The Office has rejected claims 32-41 under 35 U.S.C. § 102(b) as allegedly being anticipated by Wright *et al.*, (Crit. Rev. Immunol., 12(3,4):125-168, 1992) (*Wright*).

The rejection of claims 33-34, and 41 are moot as these claims have been cancelled. Applicants respectfully traverse the rejection of claims 32 and 35-40 for the reasons stated.

Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Foundation v. Genentech Inc.*, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991).

Claim 32 and claim 40, and the claims dependent therefrom, recite that the translation of the antibody results in secretion of the antibody from the mammalian non-plasmocyte cell into the blood circulation of a host mammal after the implantation of the mammalian non-plasmocyte cell into the host mammal.

Wright does not disclose the present invention, as claimed herein. *Wright* is a review article that explains the optimization of the *in vitro* production of monoclonal antibodies and their

purification form culture supernatants. Applicants maintain their argument that *Wright* does not anticipate the claims because this reference only provides teaching for the *in vitro* production of monoclonal antibodies.

Further, the cells used for antibody production in *Wright*, *e.g.*, c6 glioma, PC12 pheochromocytoma, HeLa, and CHO cells, are all transformed cell lines. The cell lines used in *Wright*, when administered to a subject animal, for example a mouse, end up causing tumors in that subject animal. Thus, these cells are not therapeutic, and in fact are disease-causing when administered to an animal. In contrast, Applicants disclose and claim therapeutic mammalian non-plasmocyte cells for implantation in a mammal.

Moreover, the Office points to the abstract of *Wright* as disclosing "non-plasmacyte cells which contain heterologous polynucleotide sequences which express and secrete an antibody." The abstract, however, does not mention either "non-plasmacyte cells" or the "secretion of antibodies." The *Wright* reference furthermore does not teach that the non-plasmocyte cells expressing antibody molecules result in secretion of the antibody into the blood circulation of a mammal upon implantation. Rather, the abstract generally describes the construction and expression of antibodies with a variety of modifications and suggests that "careful analysis and comparison of effector functions among immunoglobulin isotypes may be applied to the design of effective therapeutic antibodies." Unlike the modified antibodies described by *Wright*, the claimed invention recites that the "polynucleotide sequence encoding the antibody is not modified."

Accordingly, *Wright* does not disclose each claim element of the present invention, and as such cannot anticipate the present claims under 35 U.S.C. 102(b). Applicants respectfully request reconsideration and withdrawal of this rejection.

35 U.S.C. § 102 REJECTION (STEVENSON *ET AL.*)

The Office has rejected claims 32-38, 40 and 41 under 35 U.S.C. § 102(b) as allegedly being anticipated by Stevenson *et al.*, (Ann. N.Y. Acad. Sci., 772:212-226, 1995) (*Stevenson*).

The rejection of claims 33-34, and 41 are moot as these claims have been cancelled. Applicants respectfully traverse the rejection of claims 32, 35-38 and 40 for the reasons stated.

The standard for anticipation under 35 U.S.C. § 102(b) is detailed above. *Stevenson* does not disclose the present invention, as claimed herein. The Examiner references figure 1 of the *Stevenson* reference as teaching mammalian expression vectors capable of providing the expression and production of various antibodies which are secreted from cells. The results in figure 1 of the *Stevenson* reference examines the ScFv protein reactivity obtain from a bacterial expression host. These ScFv molecules comprise only a small portion, *i.e.*, fragment, of an antibody and are considered antibody derivatives. In contrast, the claims 32 and 40, as amended herein, do not encompass antibody fragments or derivatives; rather they encompass the whole antibody molecule. Indeed, the specification, *e.g.*, page 5 lines 5-10, clearly distinguishes between a therapeutic antibody from antibody fragments, *e.g.*, Fab or ScFv fragments or derivatives such as chimerical antibodies.

Furthermore, Applicants respectfully submit that a skilled artisan would not consider bacterial cells such as described in *Stevenson*, with their attendant proliferative capability and potential toxicity as "therapeutic" or suitable for administration to a mammal for *in vivo* production of therapeutic antibody as presently claimed. That is, unlike *Stevenson*, Applicants teach the use of non-plasmocyte cells. The mammalian non-plasmocyte cells recited in the claims are different than the bacterial host cells taught by *Stevenson*. As such, the claimed invention is distinct from the teachings of the *Stevenson.*

Accordingly, *Stevenson* does not disclose each claim element of the present invention, and as such cannot anticipate the present claims under 35 U.S.C. 102(b). Applicants respectfully request reconsideration and withdrawal of this rejection.

35 U.S.C. § 102 REJECTION [CHEN *ET AL.* *(1994)*; CHEN *ET AL.* *(1996)*]

The Office has rejected claims 32-37, and 39-42 under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen *et al.*, (Proc. Natl. Acad. Sci. USA, 91:5932-59-36, 1994) (*Chen I*). The Office has also rejected claims 32-37, and 39-41 under 35 U.S.C. § 102(b) as allegedly being anticipated by Chen *et al.*, (Chen *et al.*, Human Gene Therapy 7:1515-1525, 1996) (*Chen II*).

The rejection of claims 33-34, and 41 are moot as these claims have been cancelled. Applicants respectfully traverse the rejection of claims 32, 35-37, 39-40 and 42 for the reasons stated.

Chen I and *Chen II* teach the use of Fab molecules, *i.e.*, antibody fragments. Fab molecules lack the essential constant region of the immunoglobulin and are considered antibody derivatives. In contrast, the claims 32 and 40, as amended herein, do not encompass antibody fragments or derivatives; rather they encompass the whole antibody molecule. Indeed, the specification, *e.g.*, page 5 lines 5-10, clearly distinguishes between a therapeutic antibody from antibody fragments, *e.g.*, Fab or ScFv fragments. As such, the claimed invention is distinct from the teachings of the *Chen I and Chen II.*

Chen I does not anticipate the present invention. *Chen I* teaches use of COS cells (*i.e.*, SV40-transformed monkey kidney fibroblasts) and human $CD4^+$ T lymphocytes cells transfected with nucleic acid coding for Fab105 fragments using a Fab105 expression cassette with two independent CMV promoters. Claims 32, 40, 42, and the claims which depend therefrom, recite a therapeutic mammalian non-plasmocyte cell genetically modified with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence coding for a therapeutic antibody. *Chen I* does not teach these elements. The human $CD4^+$ T lymphocytes cells are not mammalian non-plasmocytes. Moreover, *Chen I* teaches away from the claimed invention. The recognized instability of the viral vectors expressing the Fab105 cassette due to recombination deletions renders them unsuited for therapeutic use. (Chen *et al.*, Human Gene Therapy 7:1515-1525, 1996; page 1518, second column, top paragraph). As such, the claimed invention, drawn to therapeutic non-plasmocyte cells and method for making and using same, is distinct from the teachings of the *Chen I.*

Accordingly, *Chen I* does not disclose each claim element of the present invention, and as such cannot anticipate the present claims under 35 U.S.C. 102(b).

Chen II also does not anticipate the present invention. The disclosure of *Chen II* teaches the use of Molt-4 human leukemic lymphoblastoid cells transfected with nucleic acid coding for Fab105 fragments using an IRES sequence derived from EMCV. Claims 32, 40, and the claims which depend therefrom, recite a therapeutic mammalian non-plasmocyte cell genetically modified with a nucleic acid, wherein the nucleic acid comprises a nucleotide sequence coding for a therapeutic antibody. This is different from the Molt-4 human leukemic lymphoblastoid host cells taught by *Chen II*. Further, Applicants respectfully submit that a skilled artisan would not consider Molt-4 human leukemic lymphoblastoid cells, with their attendant proliferative capability, as "therapeutic" or suitable for administration to a mammal for *in vivo* production of therapeutic antibody as presently claimed. As such, the claimed invention is distinct from the teachings of the *Chen II*.

Accordingly, *Chen II* does not disclose each claim element of the present invention, and as such cannot anticipate the present claims under 35 U.S.C. 102(b). Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

On the basis of the foregoing amendments, Applicants respectfully submit that the pending claims are in condition for allowance and respectfully request the same. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact either of the undersigned at the telephone number provided below.

Respectfully submitted,

Dated: May 29, 2003

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